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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,869	09/23/2003	Cyrus Rustam Kumana	UHK 00091	5138

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EXAMINER	
CHOI, FRANK I	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/669,869	KUMANA ET AL.	
	Examiner	Art Unit	
	Frank I. Choi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,28-34 and 38-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10,28-34 and 38-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/15/2007 has been entered.

Claim Rejections - 35 USC § 112/101

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 10, 28-34,38-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Applicant claims an effective amount to treat a patient in need thereof of arsenic trioxide when administered orally, wherein the amount is less than the effective amount for intravenous administration and a method of orally treatment with arsenic with fewer side effects than the same amount of arsenic trioxide administered intravenously. The Applicant cites to various pages and lines of the Specification, however, none of the same set forth the claim limitations and the Applicant does not explain how they support the same. Given that dose depends on severity of the disease condition, the patient, effect of other components on bioavailability and treatment of the disease and susceptibility of the disease to the treatment,

there is no way of determining that the amount when administered orally is less than the effective amount for intravenous administration other than a direct comparative test and such test would only be valid for the situation and formulation tested. See for example pages 24 and 25 of the Specification discussing anomalies and inter-individual variations relative to comparing oral and intravenous doses. With respect to the limitation as to having fewer side effects than the same amount of arsenic trioxide administered IV, again, the cited disclosure does not support the same. Page 28 of the Specification discloses that the side effects, including cardiac arrhythmias, were comparable between oral and IV arsenic trioxide. This does not support the fewer side effect limitation.

Further, the Applicant's citation to various references does not provide support for the claim limitations. The issue of written description is different from the issue of enablement. In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n- propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original); Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 1328, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000) ("the specification does not clearly disclose to the skilled artisan that the inventors ... considered the ratio... to be part of their invention .... There is therefore no force to Purdue's argument that the written description requirement was satisfied

because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion").

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6,9, 10, 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A single claim which claims both a product and the method steps of using the apparatus is indefinite under 35 U.S.C. 112, second paragraph. See e.g. IPXL Holdings v. Amazon.com, Inc., 430 F.2d 1377, 1384, 77 USPQ2d 1140, 1145 (Fed. Cir. 2005); Ex parte Lyell, 17 USPQ2d 1548 (Bd. Pat. App. & Inter. 1990).

The claims are also rejected under 35 U.S.C. 101 based on the theory that the claim is directed to neither a "process" nor a "machine," but rather embraces or overlaps two different statutory classes of invention set forth in 35 U.S.C. 101 which is drafted so as to set forth the statutory classes of invention in the alternative only. See e.g. Id. at 1551.

In this case, the claims require that the amount administered orally be less than the effective amount for intravenous administration. However, as indicated above, there is no way of determining the same absent direct comparative testing. See for example pages 24 and 25 of the Specification discussing anomalies and inter-individual variations relative to comparing oral and intravenous doses. As such, the claim by its terms requires method steps in order to

determine whether the orally administered amount is less than the intravenously administered amount.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4,10 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/24029.

WO 99/24029 expressly discloses a composition containing arsenic trioxide, water, NaOH and HCl, having a pH of 6.5 (Pg. 27, lines 20-38, page 28, lines 1,2).

The Examiner has duly considered the Applicant's arguments but deems them unpersuasive.

The claims are directed to a composition. The intended use of the composition does not patentably distinguish the prior art composition form the prior art. The Applicant has provided no evidence that the prior art composition cannot be administered orally. With respect to the process limitations in the composition claim, "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product

itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). The claim limitation fails to set forth any specified amount since the amount can very depending a numerous factors, including type and severity of disease, susceptibility of disease, the presence of other components, etc. The Applicant claims in claim 10, dispersions and suspensions. The Applicant, however, provides no evidence that the same excludes the prior art composition or that suspensions or dispersion cannot be administered intravenously. Clearly, the components are dispersed or suspended in the water at a molecular or ionic level. The Applicant has provided no evidence that the prior art product is different from the claimed invention.

Claims 1-4,10 are rejected under 35 U.S.C. 102(a) as being anticipated by CN1370540 (Abstract).

CN1370540 (Abstract) expressly discloses a composition containing arsenic trioxide, water, NaOH and HCl and a pH of 7.2-7.4.

The Examiner has duly considered the Applicant's arguments but deems them unpersuasive for the same reasons as above.

With respect to the rejection below, the Examiner has withdraw the rejection solely as to the method claims as the prior art does not disclose that the effective oral doses has fewer side effects than the same amount administered intravenously.

Claims 1-6, 9, 10,44 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/24029 and CN1370540.

WO 99/24029 disclose treatment of leukemia with neutralized solution containing arsenic trioxide, NaOH and HCl. (WO 99/24029, see entire document, especially, Pg. 14, lines 18-38, Pgs. 15-41, Claims 16-18). One product is disclosed as having a pH of 6.5 (Pg. 27, lines 20-38, page 28, lines 1,2). It is disclosed that the composition can be administered orally, including in the form of tablets and suspension, and with other chemotherapeutic drugs (Page 7, lines 31-38, Page 17, lines 14-34, pg. 19, lines 4-37). It is disclosed that the daily dose ranges from about 0.05 to about 5 mg/kg body weight administered and that the preferred total daily dose is from 2.5 to about 40 mg of arsenic trioxide (Page 17, lines 14-34).

CN1370540 disclose treatment of leukemia with neutralized solution containing arsenic trioxide, NaOH and HCl (CN1370540, Abstract).

The prior art discloses treatment of leukemia with neutralized solution containing arsenic trioxide, NaOH and HCl that can be administered orally. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose oral formulation having an amount that is less than the effective amount for intravenous administration. However, the prior art amply suggests the same as the prior art discloses oral formulations and amounts to be administered daily. As such, it would have been well within the skill of one of ordinary skill in the art to prepare an oral formulation containing any amount of arsenic trioxide as desired to depending on the particular formulation and amount necessary to effectively treat the leukemia. The limitation indicated above fails to specify any specific amount and is so broad as to practically encompass any amount.

The Examiner has duly considered the Applicant's arguments but deems them unpersuasive for same reasons as above, the reasons of record set forth in the prior Office Action (2/7/2007), and the further reason below.

The Supreme Court in KSR International Co. v. Teleflex Inc., held that (1) it is error to look only the problem the patentee was trying to solve-any need or problem known in the filed of endeavor at the time of invention and addressed by the prior art can provide a reason for combining the elements in the manner claimed; (2) it is error to assume that one of ordinary skill in the art in attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem-common sense teaches that familiar items may have obvious uses beyond their primary purposes, and in many cases one of ordinary skill in the art will be able to fit the teachings of multiple patents together like pieces of a puzzle (one of ordinary skill in the art is not automaton); (3) it is error to assume that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try". KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385, 1397 (U.S. 2007).

The Applicant argues that topical and inhalation is impossible. Notwithstanding that the Applicant is not claiming these routes of administration, the Applicant has not provided any evidence the same is impossible. Further, the Applicant has provided not provided any evidence with respect to oral versus intravenous bioavailability or mucositis caused by chemotherapeutic drugs. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). Further, the Applicant's determination as

to greater than 90% bioavailability appears to be based on supposition. In the experiment in the Specification, the oral dose was given after IV dosing. Since the patient has received arsenic via IV, a measurement of blood plasma levels is not accurate assessment as to the bioavailability of the second dose given orally. Further, the Specification indicates that there was considerable inter-individual variations in plasma and whole blood AUCs and that dosage/drug level relationships to the efficacy and toxicity of arsenic trioxide needs further exploration. See Specification pages 24, 25. In any case, in view of the fact that WO 99/24029 does disclose oral administration, the Applicant's conclusion that one of ordinary skill in the art would not orally administer the same is without merit. The Applicant argues that one or ordinary skill in the art would expect that one would need a much larger dosage not a lower dosage. Even if true, this has no practical significance in a composition claim in that the claimed limitation does not exclude any specified amount since the amount effective orally can vary as can the amount effective intravenously. The Applicant's speculation as to what the inventors in WA 99/24029 would or would have not done is not sufficient to overcome the rejection. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Since the prior art does teach oral administration of arsenic trioxide for treatment of leukemia, contrary to the Applicant's arguments, there is a reasonable expectation of success.

The Applicant submit various references as evidence of unexpected activity, however, evidence of unexpected activity must be by affidavit or declaration. See Ex parte Gray, 10 USPQ2d 1922, 1928 (Bd. Pat. App. & Inter. 1989) ("The reason for requiring evidence in declaration or affidavit form is to obtain the assurances that any statements or representations

made are correct, as provided by 35 U.S.C. 25 and 18 U.S.C. 1001." Permitting a publication to substitute for expert testimony would circumvent the guarantees built into the statute.).

In any case, the Applicant's references are not sufficient to overcome the prima face case of obviousness. The Applicant argues that the standard oral dose is equal to or less than 5 to 10 mg with greater than 90% availability. However, the Applicant does not cite to evidence that supports the same. Applicant's specification states that the total daily dose range of arsenic trioxide varies on various factors, but that generally the dose is about 1,2,3,4,5,6,7,8,9,10,15,20 or 25 mg/day, preferably, about 10 mg/day in single or divided doses (Specification, page 9). The Specification also discloses that capsules can contain 0.25, 0.5, 1,5,10,15,20,25,30,40 or 50 mg of arsenic trioxide in powdered form (Specification, page 12, lines 25-29). In any case, the Applicant tested solutions containing water, sodium hydroxide, arsenic trioxide and HCl in specified amounts. As such, even if the offered references were valid submission of evidence, the claims are broader in scope and, thus, the alleged evidence is not commensurate in scope with the claims. In any case, with respect to the composition claims, none of the alleged evidence provided establishes that the preparation of oral dosage forms are outside the capabilities of one of ordinary skill in the art. See Pfizer Inc. v. Apotex Inc., 82 USPQ2d 1321, 1338 (Fed. Cir. 2007) (Even though applicant's modification result in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one of ordinary skill in the art).

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been taught by the teachings of the cited reference.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Thursday, Friday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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June 24, 2007

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